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PRINCIPAL INVESTIGATOR: Nicholas Daniels, MD MPH

CONTRACTING ORGANIZATION: Regents of the University of California
                                                San Francisco CA 94143-0962

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E-Mail: ndaniels@medicine.ucsf.edu

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14. ABSTRACT
Chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS) is a major cause of illness and the association with past urinary tract infections is unclear. We surveyed a racially, ethnically and socioeconomically diverse, community-based sample of adults aged 30–79 years in Boston, Massachusetts. This report gives estimates from the 2301 men in the BACH survey: 700 Black, 766 Hispanic, and 835 White. Symptoms of chronic prostatitis—any perineal and/or ejaculatory pain and a pain score of 4 or greater—were derived from the NIH Chronic Prostatitis Symptom Index and were used to identify men with symptoms suggesting CP/CPPS. The overall prevalence of symptoms suggestive of CP/CPPS is 6.3%. The number of urinary tract infections, particularly more than three, was associated with these symptoms suggestive of CP/CPPS (P<.01). There is a strong association between current symptoms of CP/CPPS and a history of urinary tract infections, particularly of multiple infections. The causality between chronic UTIs and CP/CPPS needs to be clarified by further study.

15. SUBJECT TERMS
Urinary tract infection (UTI), chronic prostatitis, prostate cancer

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INTRODUCTION

Chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS) is a common urologic problem that impairs quality of life in men and that is difficult to treat.[1–3] There is scant evidence about potential, particularly modifiable, risk factors for the development of chronic prostatitis symptoms.[4,5] Further identification and characterization of important risk factors could lead to the development of risk reduction strategies.

The National Institutes of Health (NIH) classifies prostatitis syndromes as acute bacterial, chronic bacterial, CP/CPPS, and asymptomatic inflammatory prostatitis.[6] The most common is CP/CPPS, which is characterized by persistent discomfort or pain in the pelvic area and/or ejaculatory pain. The cause of CP/CPPS is unknown; few studies have explored its risk factors, and treatment with antimicrobial agents and alpha-blockers has not shown significant improvement in symptoms or quality of life.[7,8]

The objective of this report is to describe the prevalence; the distribution by race/ethnicity, age, and socioeconomic status (SES); and the association of current symptoms of CP/CPPS with a history of urinary tract infections (UTIs) and prostate cancer in a community-based random sample of men.

BODY

The Boston Area Community Health (BACH) survey is designed to estimate the prevalence of symptoms of

urological disorders in a multi-ethnic, community-based sample of adults aged 30–79 years. Using a stratified cluster

sample, 5506 adult men and women were recruited in three racial/ethnic groups: Hispanic, Black, and White. This

report is based on the 2301 men included in the BACH study: 700 Black, 766 Hispanic,

and 835 White.

Overall Design

The BACH study is a population-based, random-sample, epidemiologic survey of a broad range of urologic and

urogynecologic symptoms that is funded by the National Institute of Diabetes and Digestive and Kidney Diseases

(NIDDK), National Institutes of Health (NIH). The research design called for equal numbers of subjects in each of

24 design cells defined by age (30–39, 40–49, 50–59, and 60–79 years), sex, and race/ethnicity (Black, Hispanic,

and White). The BACH two-stage, stratified cluster sample (n=5506) was recruited from April 2002 through June

2005.

Stratified, Two-Stage Cluster Sample

For the study, the city of Boston was divided into four geographic areas and three levels of minority density (a total

of 12 strata). The levels of minority density were low-density minority (primarily White), high-density Black (at

least 25% of the residents were Black), and high-density Hispanic (at least 30% of the residents were Hispanic).

Census blocks were randomly sampled from 4266 blocks in the city of Boston by stratum such that approximately

10% of the low-density minority blocks, 15% of the high-density Black blocks, and 75% of the high-density

Hispanic blocks were selected.

Sampling proceeded in five batches, each a random subsample (or "mini-version") of the overall BACH study.[9]

Households from selected census blocks were identified using a current Boston Resident List that had been

geocoded (Caliper, Newton, MA) with census tract and block information for each individual. Telephone numbers

were obtained from a telephone matching service (Telematch Gannett, Springfield, VA) for approximately half of

the selected individuals. One individual per household was designated as the primary contact person, with

preference given to a person with a telephone number. Introductory letters were mailed to the selected households requesting a contact telephone number, if not already available (47.5% of the households). Households were screened either by telephone or by a field visit (if screeners were unable to reach the household by telephone). Screening was completed for 36% of the selected households; 30% of the households refused screening and 34% of the households could not be contacted after 10 telephone calls, three mailings, and three field visits (16 attempts to reach them).

Individuals from the selected census blocks were chosen according to eligibility rules to achieve our goal of approximately equal numbers of Black, White, and Hispanic respondents by sex in four age categories: 30–39, 40–49, 50–59, and 60–79 years. Some of the eligibility rules used in BACH were any age-eligible subject and any age-eligible Black or Hispanic male subject. Eligibility rules varied by batch and were randomly assigned to selected households based on household demographics at the start of each batch. BACH inclusion criteria included self-identified as Black, White, or Hispanic race/ethnicity, aged 30–79 years, competent to sign informed consent, and able to speak English or Spanish well enough to complete the survey. In total we recruited 5506 people: 2301 men and 3205 women consisting of 1770 Blacks, 1877 Hispanics, and 1859 Whites. Interviews were completed with 63.3% of the screener-identified eligible individuals from the selected households. Of the 5506 interviews, 1461 (26.5 %) were conducted in Spanish, mostly with Hispanic subjects.

Because of design requirements, the BACH subjects had unequal probabilities of selection into the study. For analyses to be representative of the city of Boston, it was necessary to weight observations inversely proportional to their probability of selection into the study.[10,11] Weights were further post-stratified to the population of Boston according to the 2000 Census. Demographics and basic health-related variables were compared between BACH and the Boston sample of the BRFSS, and results were found to be comparable. Basic health-related variables were compared between BACH and national government surveys (NHIS – National Health Interview Survey: http://www.cdc.gov/nchs/nhis.htm, NHANES – National Health and Nutrition Examination Survey: http://www.cdc.gov/nchs/nhanes.htm, BRFSS – Behavioral Risk Factor Surveillance System: http://www.cdc.gov/brfss/) and the results were found to be comparable, indicating that the results from BACH may be generalizable to the country as a whole.

Data Collection

Data were obtained during a 2-hour, in-person interview, generally conducted in the subject's home by a well-trained (bilingual) interviewer.[12] Following written informed consent (all protocols and informed consent procedures were approved by New England Research Institutes [NERI] Institutional Review Board), anthropometric measurements (blood pressure, height, and weight) were obtained, along with information on medical (sexually transmitted diseases, kidney infections, vasectomy, alcohol use and smoking habits) and reproductive history, major co-morbidities, prescription and over-the-counter medications, lifestyles, psychosocial factors, medical care utilization, and detailed self-reported major symptoms of seven different urogynecologic conditions (urinary incontinence, benign prostatic hyperplasia, interstitial cystitis/chronic pelvic pain, prostatitis, hypogonadism/androgen deficiency, erectile dysfunction, female sexual dysfunction). Wherever possible, the questions and scales employed on BACH were selected from published instruments with documented metric properties and, following some minor modifications, were approved by a Scientific Advisory Committee of experts in urology and urogynecology. To ensure acquisition of the highest quality data, all staff were trained, certified, monitored, and regularly retrained in all procedures and protocols. A minimum of 10% double data entry helped ensure accurate data computerization. Regular reports from NERI's electronic data capture ADEPT software (NERI, Watertown, MA) closely monitored all aspects of data completeness and quality.

Variables of Interest

The BACH survey includes modified NIH Chronic Prostatitis Symptom Index (NIH-CPSI)[13] questions that pertain to urogenital pain and urinary symptoms during a time frame of 1 month. The longer time frame from the standard 1-week period may increase the prevalence of these symptoms. Any perineal and/or ejaculatory pain and a CPSI pain score of 4 or greater were used to identify men who had symptoms suggesting prostatitis.[14,15] Socioeconomic status (SES) was determined using a combination of education and income[16] and categorized such that 25% of the population was of lower, 50% of middle, and 25% of upper socioeconomic status. Quality of life was measured by the SF-12 instrument and converted to physical and mental health component scores.[17] In the baseline questionnaire, participants were asked: "Have you ever been told by your health care provider that you had a bladder infection

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(urinary tract infection or cystitis) or kidney infection (pyelonephritis)?" If they answered "yes," they were also asked: "How many times were you diagnosed with a bladder infection (urinary tract infections or cystitis) in your lifetime?"

Statistical Analyses

Multiple imputation (MI) was used to impute missing values using the procedure in SAS version 9.1 (SAS Institute Inc, Cary, NC).[18–20] Statistical analyses taking into account the two-stage cluster survey design using sampling weights were performed using SUDAAN version 9.0.1 (Research Triangle Institute, Research Triangle Park, NC).[21] The strength of the association of symptoms suggestive of CP/CPPS and categorical variables was measured by a χ^2 statistic. Analysis of variance was used to measure the association of symptoms of prostatitis and continuous variables. A multiple logistic regression model was used to model the overall association of symptoms of CP/CPPS and multiple covariates and was used to calculate the odds ratios and 95% confidence intervals.

Covariates (Table 2) were entered as categorical variables with the exception of SES, which was entered as a continuous variable. Keeping age group and race/ethnicity in the model, covariates were removed using backwards elimination. Covariates were kept in the model if $P<0.05$ overall or for at least one racial/ethnic group.

KEY RESEARCH ACCOMPLISHMENTS

Demographic and some health characteristics for the BACH sample are reported in Table 1. The overall prevalence of symptoms suggestive of CP/CPPS was 6.3%. Table 2 gives bivariate associations of symptoms suggestive of CP/CPPS with categorical variables and Table 3 with continuous variables. In bivariate analyses, symptoms suggestive of chronic prostatitis increased with age, were not different by race/ethnicity, and increased with lower socioeconomic status (although this was not statistically significant). Twenty-one percent of respondents with a history of prostate cancer had symptoms of chronic prostatitis compared with only 6% of those without a history of prostate cancer ($P=.04$). Of men with a history of a sexually transmitted disease, 7.6% had symptoms of chronic prostatitis compared with 6% of those without a history of a sexually transmitted disease ($P=.38$) [data not shown]. Symptoms of CP/CPPS were seen in 5.7% of respondents without a history of UTIs compared with 7.3% of those with one UTI, 10.3% of those with two, and 27.2% of those with three or more ($P=.19$) (Figure). Persons with

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symptoms of chronic prostatitis had significantly lower physical and mental health component scores and significantly greater numbers of health care provider visits in the past year.

REPORTABLE OUTCOMES

In a multiple logistic regression model (Table 4), the number of UTIs in a patient's history was associated with symptoms suggestive of CP/CPPS (P=0.0075). Men with three or more UTIs had almost 5-fold higher odds of having symptoms suggestive of chronic prostatitis/chronic pelvic pain compared with men without a history of multiple UTIs. An overall trend was noted between a history of prostate cancer and CP/CPPS (P=.09) after adjusting for age, race/ethnicity, and number of UTIs. The association between UTIs and chronic prostatitis symptoms was stronger for Whites (P=0.003), than for Blacks or Hispanics, while the association between prostate cancer and symptoms suggestive of CP/CPPS were stronger for Blacks (P=0.03), than for Whites or Hispanics.

CONCLUSIONS

This study from the BACH survey—one of few racially and ethnically diverse community-based U.S. samples to examine a broad range of urological symptoms suggestive of different urologic diseases—found a strong association between current symptoms suggestive of CP/CPPS and a self-reported history of UTIs, particularly for Whites. This association is biologically plausible because the mechanisms of bacterial prostatitis (acute and chronic) are believed to include ascension of urethral microbes or reflux of urine from the bladder into the prostate, with subsequent infection and/or inflammation of the prostate.[22] The mechanism or role of infection in CP/CPPS (category III) patients in our study, however, is unclear. To our knowledge, this study may be the first to demonstrate a clear association between an increasing number of past UTIs and symptoms suggestive of current CP/CPPS. A recently published case-control study examining risk factors for CP/CPPS also found that men with the syndrome were significantly more likely to have a history of UTIs.[23]

Prior studies have shown that lack of circumcision increases the risk of UTIs in men, along with unprotected sexual intercourse, benign prostatic hyperplasia, renal stones, increasing age, and urethral instrumentation.[24–29] In contrast to women, very little is known about UTIs in men,[30,31] partly due to their low incidence.[32] In our population from the BACH survey, 9.0% of men had a history of one or more UTIs. Current research on UTIs in men shows that men and women have similar infecting bacterial species, host predispositions, and treatment results.[33] One important and obvious difference is the presence of a prostate gland in men and poor antimicrobial penetrance into this gland. Total annual health care expenditures are slightly higher for men than for women with UTIs ($5,544 vs. $5,407 per year) and mean time lost from work due to cystitis is also higher for men (10.5 vs. 4.8 hours).[34]

The NIH-CPSI, a validated symptom index, is used in men with symptoms suggestive of CP/CPPS to quantify symptoms and response to treatment. The questionnaire has been proven to have a high degree of internal consistency and reliability when self-administered in clinical practice for patients with chronic prostatitis.[35] The NIH-CPSI total score has been accepted as a reliable outcome measure for prostatitis treatment in primary and secondary care patients with varying duration of prostatitis-like symptoms, and supplementation with measures of pain intensity and activity may improve its usefulness.[35] We used any perineal and/or ejaculatory pain and a pain score of 4 or greater, as previously done in the medical literature, to identify men with symptoms suggesting

CP/CPPS and to distinguish them from normal controls and men with benign prostatic hyperplasia.[14,15] It is important to note that our study may overestimate the prevalence or symptoms suggestive of CP/CPPS since we used a modified NIH-CPSI tool by altering the order of symptom query in our survey instrument and by using a 1-month period instead of 1-week period (as used by Roberts et al), which may have allowed us to identify more men with chronic prostatitis–like symptoms. Although, in our study, the overall prevalence of symptoms suggestive of CP/CPPS was 6.3%, which is within the range of overall prevalence of prostatitis previously estimated at between 2% and 16%.[2,14,15,36–39]

History of prostate cancer also had an overall association with symptoms suggestive of chronic prostatitis in our multivariate model (statistically significant only for Blacks), although it is unknown whether the onset of CP/CPPS symptoms preceded the cancer diagnosis. It is unclear how the higher incidence of prostate cancer among Blacks affects symptoms suggestive of CP/CPPS. The lack of overall significance may be related to the small number of persons with a history of prostate cancer (n=50). Associations between prostate cancer and chronic prostatitis have been reported, but the exact relation has not been well characterized. It is clear that lower urinary tract symptoms or symptoms of prostatitis may prompt prostate-specific antigen testing and digital rectal examination, which increases the likelihood of a prostate cancer diagnosis. On the other hand, data increasingly suggest that inflammation of the prostate may promote carcinogenesis, similar to the association of inflammation with other cancers.[40–42] Current symptoms of CP/CPPS were associated with an increased number of health care provider visits in the past year and with decreasing physical and mental health component scores. These findings suggest that persons with more severe symptoms suggestive of CP/CPPS tend to see providers more often and to have lower physical and mental health scores, possibly due to their age and/or co-morbid problems which increase the likelihood of social isolation and reduce physical activity or because CP/CPPS symptoms decrease overall quality of life.

Our study has several limitations. Because of the cross-sectional nature of the data, our findings do not suggest causality but call for additional research into the relation of a history of UTIs and current CP/CPPS symptoms. There are plans for BACH to evolve into a prospective cohort study. Moreover, it is possible that misclassification may have occurred if physicians labeled early symptoms suggestive of CP/CPPS as UTIs. The reliability of self-report (e.g., questionnaires) of chronic prostatitis symptoms and UTIs is largely unknown in a community-based

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population. Because CP/CPPS in particular is often a clinical diagnosis of exclusion and therefore is difficult to definitively diagnose, respondents may have reported an incorrect diagnosis of UTI. Alternatively, the strengths of the study lie in the large sample size of different racial, ethnic and socio-economic groups; the random selection of study participants from the general community, and the emphasis on urological symptoms rather than diagnosed diseases.

In conclusion, these results show that an increasing number of past UTIs is positively associated with symptoms suggestive of CP/CPPS. Reduction of recurrent UTIs may decrease the development of CP/CPPS symptoms. Clinicians might consider ordering a urine culture and consider the diagnosis of UTI when men are seen with a urethritis presentation. Our study was not designed to demonstrate modification of risk factors for symptoms of CP/CPPS. Nevertheless, it is prudent to recommend that patients take precautions, such as using protective barriers during sexual intercourse and seeking care for symptoms of bladder obstruction, to reduce exposure to microbes that can cause UTIs. Further study is needed to determine if prevention of recurrent UTIs can reduce the risk of CP/CPPS symptoms and to clarify causality between chronic UTIs and CP/CPPS.

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Table 1. Characteristics of the 2301 Men in the BACH Survey—Weighted to the Population of Boston

Characteristics	Men	Black Men	Hispanic Men	White Men	*P* Value
			Percent		
Born in United States	77.5	75.5	15.9	91.2	<.0001
Years of Education (12 or fewer)	33.0	45.9	66.1	20.8	<.0001
Socioeconomic Status					<.0001
Lower	24.0	36.9	58.4	11.6	
Middle	49.2	53.2	30.4	51.5	
Upper	26.8	9.9	11.2	36.8	
Marital Status (married or living with a partner)	55.3	47.2	64.3	56.6	.0002
Health Insurance					<.0001
Private	67.4	56.7	43.2	76.8	
Public (Medicare, Medicaid) Only	19.9	27.2	26.2	12.5	
None	14.7	16.1	30.7	10.7	
Smoking Status					.0003
Never	38.8	40.4	48.9	36.1	
Former	28.9	22.3	25.0	32.4	
Current	32.3	37.3	26.0	31.5	
Body Mass Index					.0437
<25	26.5	27.4	26.4	26.2	
25-30	40.8	33.8	42.0	43.4	
30+	32.7	38.8	31.6	30.4	
General Health Status					<.0001
Excellent	20.0	15.6	15.0	22.9	
Very Good	33.6	29.4	21.4	37.8	
Good	31.5	36.6	33.6	29.0	
Fair	11.7	14.7	27.1	7.2	
Poor	3.3	3.8	2.9	3.1	
Number of Urinary Tract Infections					.2512
0	91.0	92.0	93.7	90.1	
1	4.6	4.1	2.8	5.2	
2	2.2	1.3	2.0	2.5	
3+	2.2	2.7	1.5	2.2	
Prostate Cancer	1.8	2.1	1.0	1.9	.3804

BACH = Boston Area Community Health

Table 2. Symptoms Suggestive of Chronic Prostatitis/Chronic Pelvic Pain Syndrome by Characteristics of the 2301 Men in the BACH Study—Weighted to the Population of Boston

Characteristics	Men			Black Men			Hispanic Men			White Men		
	%	s.e.	*P Value*	%	s.e.	*P Value*	%	s.e.	*P Value*	%	s.e.	*P Value*
Race/ Ethnicity			.8902									
Black	6.35	1.10										
Hispanic	5.70	1.27										
White	6.41	1.28										
Age Group (years)			.1170			.0301			.5151			.3993
30–39	3.96	1.53		2.00	1.40		4.23	1.68		4.63	2.21	
40–49	5.29	1.31		6.98	2.18		5.27	2.55		4.48	1.92	
50–59	8.06	1.80		9.05	3.11		9.30	3.76		7.40	2.48	
60–79	10.59	2.49		10.90	3.28		8.36	3.39		10.70	3.37	
Socioeconomic Status			.5925			.2366			.7919			.7762
Lower	7.69	1.49		8.16	2.23		6.08	1.64		8.81	3.76	
Middle	6.13	1.06		5.77	1.67		5.80	2.53		6.32	1.48	
Upper	5.37	1.99		2.71	2.41		3.42	3.39		5.78	2.31	
History of Prostate Cancer			.0437			.0563			.8928			.2883
Yes	20.93	7.46		36.16	13.94		6.58	7.00		15.66	8.99	
No	6.03	0.86		5.71	1.07		5.69	1.28		6.23	1.28	
History of Urinary Tract Infection			.0519			.2845			.3040			.1062
Yes	12.87	3.54		12.58	5.72		12.71	7.13		12.98	5.69	
No	5.65	0.85		5.80	1.15		5.22	1.21		5.69	1.25	
Smoking Status			.3833			.4713			.8737			.3806
Never	5.01	1.09		5.62	1.66		6.37	2.26		4.34	1.60	
Former	7.15	1.92		4.73	2.13		4.99	1.76		8.18	2.67	
Current	7.10	1.41		8.11	2.11		5.11	1.52		6.96	2.25	

BACH = Boston Area Community Health; s.e. = standard error.

Table 3. Association of Continuous Variables and Symptoms Suggestive of Chronic Prostatitis/Chronic Pelvic Pain Syndrome in the 2301 Men from the BACH Survey—Weighted to the Population of Boston

Symptoms Suggestive of CP/CPPS	Men			Black Men			Hispanic Men			White Men		
	Yes	No	P Value	Yes	No	P Value	Yes	No	P Value	Yes	No	P Value
Continuous Variables												
Age (years)			.0192			.0014			.1112			.1631
Mean	52.28	47.31		54.33	47.27		47.81	44.03		52.29	48.03	
standard error	2.03	0.47		2.08	0.72		2.31	0.54		2.94	0.69	
Physical Health Component Score			<.0001			<.0001			.0012			.0065
Mean	43.68	50.71		39.78	1.81		42.46	50.49		45.48	51.28	
standard error	1.46	0.32		49.40	0.57		2.34	0.50		2.10	0.45	
Mental Health Component Score			.0002			.0063			.0029			.0130
Mean	44.74	50.75		44.13	2.18		43.49	51.16		45.23	50.84	
standard error	1.52	0.37		50.32	0.57		2.45	0.52		2.16	0.53	
Number of Visits to HCP in the Past Year			.0003			.0337			.0522			.0101
Mean	14.38	7.42		12.16	6.76		9.84	4.66		16.14	8.28	
standard error	1.86	0.48		2.39	0.66		2.62	0.44		2.93	0.73	

BACH = Boston Area Community Health; CP/CPPS = Chronic prostatitis/chronic pelvic pain syndrome; HCP = health care provider

Table 4: Results from a Logistic Regression Model for Symptoms Suggestive of Chronic Prostatitis/Chronic Pelvic Pain Syndrome in the 2301 Men from the BACH Survey

Characteristic	Men			Black Men			Hispanic Men			White Men		
	Odds Ratio	95% Confidence Interval	*P Value*	Odds Ratio	95% Confidence Interval	*P Value*	Odds Ratio	95% Confidence Interval	*P Value*	Odds Ratio	95% Confidence Interval	*P Value*
Race/Ethnicity			.9777									
Black	1.00	0.56, 1.78										
Hispanic	1.06	0.59, 1.89										
White	1.00	reference										
Age Group (years)			.2585			.4670			.5719			.4991
30–39	1.00	reference		1.00	reference		1.00	reference		1.00	reference	
40–49	1.29	0.50, 3.32		3.75	0.64, 22.15		1.20	0.33, 4.31		0.85	0.23, 3.20	
50–59	1.93	0.75, 4.96		4.65	0.68, 31.79		2.44	0.65, 9.15		1.34	0.37, 4.82	
60–79	2.36	0.86, 6.49		4.97	0.63, 31.79		1.85	0.50, 6.79		1.98	0.55, 7.06	
History of Urinary Tract Infections			.0075			.7986			.5056			.0034
0	1.00	reference		1.00	reference		1.00	reference		1.00	reference	
1	1.30	0.50, 3.39		2.07	0.40, 10.78		1.92	0.37, 9.99		0.82	0.18, 3.64	
2	1.50	0.48, 4.63		0.55	0.04, 10.78		3.79	0.57, 25.06		1.45	0.30, 6.92	
3+	4.91	1.95, 12.40		1.36	0.15, 12.37		2.04	0.19, 21.94		8.34	2.69, 25.90	
History of Prostate Cancer	2.41	0.87, 6.64	.0897	7.37	1.24, 43.91	.0327	1.03	0.12, 8.55	.9758	1.33	0.29, 6.04	.7145

BACH = Boston Area Community Health.

Figure: Prevalence of Symptoms Suggestive of Chronic Prostatitis/Chronic Pelvic Pain Syndrome by Number of Urinary Tract Infections in the 2301 Men from the BACH Survey